Comments of Katharine Young

Comment 1:

There have been a number of recent reviews of the association between SIDS and parental smoking[1,8,20,28]. When attempting to interpret the results relating to ETS exposure it is important to bear in mind the following points:

Some of the studies[10,11,13,25] reporting an association between SIDS and ETS exposure have not adjusted for any other risk factors, while many others[9,12,14,16,17,21,23,26,27] have only taken a few of them into account.

Response:

Consideration of other risk factors is a critical concern, especially in many of the older studies mentioned above. In general, the more recent studies included in this update had better control for confounding and continued to support a causal association.

Comment 2:

Four studies[15,18-20] have taken into account quite an extensive list of potential confounding variables in at least some of their analyses. In two studies[15,20], such adjustment explained about 80% of the increased risk of SIDS associated with maternal smoking after pregnancy, and in a third study[19] it explained about 50%. In the fourth study[18], adjusted results were not reported for maternal smoking after pregnancy, but adjustment markedly reduced the relative risk associated with maternal smoking in pregnancy, from 4.84 to 1.78. Since such adjustments will inevitably be incomplete - partly because not all such factors will have been considered, and partly because data errors or use of surrogate variables limit the ability to control for confounding - it is not implausible that all of the claimed SIDS/ETS association could in fact be explained by confounding.

Response:

Newborns are indeed vulnerable to a variety of environmental conditions that may contribute to SIDS, adjustment for which reduces the apparent risks associated with ETS. However the consistency of the association of SIDS with ETS exposure in a variety of studies after adjustment for multiple confounders reduces the plausibility that the SIDS/ETS association is wholly explainable by confounding. Furthermore, adjustment for all confounders is nearly impossible, and may actually result in over-controlling for confounders masking the ETS effect.

Comment 3:

In a recent study[29], infants with prolongation of the QT interval, as measured by electrocardiograph shortly after birth, had a more than 40-fold increased risk of SIDS. This abnormality, seen in 50% of the infants dying of SIDS, is a major risk factor that could not have been caused by postnatal ETS exposure and which has not been taken account of in any of the epidemiological studies of ETS and SIDS.

Response:

Recent experiments in rats may provide a link between an infant's smoke exposure in utero and prolonged QT interval. Alterations in cardiovascular responsiveness to neurotransmitters were seen in rats after prenatal exposure to nicotine at levels consistent with maternal smoking (Slotkin et al., 1999). This exposure was associated with an increase in cardiac muscarinic type 2 receptors (M2) on which acetylcholine acts to decrease contraction rate. Nicotine exposure has been shown previously to cause a decrease in ß-adrenergic receptors (Navarro et al., 1990) through which heart rate is stimulated. The combination of an increase in inhibitory receptors and a decrease in excitatory receptors would be expected to lead to dis-regulation of heart function, possibly manifesting as an increased QT interval. This study also reported a nicotine-induced reduction in brainstem muscarinic receptors paralleling that seen in infants who have died from SIDS. In these infants there was decreased binding in brainstem areas associated with cardiorespiratory functions (Kinney et al., 1995). Thus ETS exposure may contribute to the risk of SIDS by impairing the ability of the brain and heart to respond appropriately to periods of hypoxia especially in infants exposed to smoke components in utero.

Comment 4:

Even if the association between parental smoking and SIDS cannot fully be explained by uncontrolled confounding by other risk factors, it may result, not from ETS exposure but from an effect of maternal smoking in pregnancy. Some studies have found that the association of SIDS with postnatal maternal smoking or paternal smoking has been reduced[15,16,20] or even eliminated[21] if adjustment is made for maternal smoking in pregnancy or if attention is restricted to nonsmoking mothers, though others have not[14,19].

Response:

Infants whose mothers smoked during pregnancy are indeed at greater risk of dying from SIDS; however, postnatal ETS exposure is an independent risk factor that can exacerbate this effect.

Thus a reduction in the apparent SIDS risk after adjustment for maternal prenatal smoking would be expected. Our estimate of SIDS risk for maternal postnatal smoking is from a meta-analysis of studies that controlled for maternal prenatal smoke exposure (Anderson and Cook, 1997). Yet higher risks (OR 3.50) and a dose response were found by Klonoff-Cohen et al (1995) for postnatal ETS from all sources after adjusting for maternal prenatal smoking and other risk factors.

References used in responses:

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Klonoff-Cohen HS, Edelstein SL, Lefkowitz ES, Srinivasan IP, Kaegi D, Chang JC, et al. (1995). The effect of passive smoking and tobacco exposure through breast milk on sudden infant death syndrome. JAMA 273(10):795-8.

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Slotkin TA, Epps TA, Stenger ML, Sawyer KJ, Seidler FJ (1999). Cholinergic receptors in heart and brainstem of rats exposed to nicotine during development: implications for hypoxia tolerance and perinatal mortality. Brain Res Dev Brain Res 113(1-2):1-12.